

Process for the efficient preparation of N-substituted dehydroamino acid esters

Description of Technology: Dehydro .alpha.-amino acids are key intermediates for the manufacture of unnatural D-.alpha.-amino acids and non-proteinaceous .alpha.-amino acids using asymmetric hydrogenation technology. Such amino acids are increasingly important intermediates in the pharmaceutical, agrichemical, and flavor/fragrance industries. For example, the amino acid D-alanine is a component of an artificial sweetener alitame while non-proteinaceous 2-aminobutyric acid is a component of a tuberculostatic drug ethambutol.

Patent Listing:

1. **US Patent No.** 5,559,268, Issued on September 24, 1996, "Process for the efficient preparation of N-substituted dehydroamino acid esters."

http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HTTOFF&p=1&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=1&f=G&l=50&co1=AND&d=PTXT&s1=5,559,268.PN,&OS=PN/5,559,268&RS=PN/5,559,268

Market Potential: Existing procedures for the dehydration of .beta.-hydroxy-.alpha.-amino acids fall into two categories, namely stepwise processes and direct dehydration procedures. In the stepwise routes, the hydroxyl group is often first converted to a better leaving group, typically the p-toluenesulfonate. Alternatively, the hydroxyl group has been O-diphenylphosphorylated for this purpose. Both procedures utilize moisture-sensitive derivatizing agents. Another stepwise process involves activation of the amine functionality by converting it to a cyclic diamide, followed by dehydration using the acidic catalyst potassium bisulfate. A. G. Brown and T. C. Smale, J. Chem. Soc., Perkin Trans. 1, 65 (1972). All of these stepwise procedures are inherently inefficient since they involve the isolation and purification of a reactive intermediate.

Most of the direct dehydration processes utilize expensive reagents such as diisopropylcarbodiimide/copper(I) chloride, N,N'-carbonyldiimidazole, or DAST (diethylaminosulfur trifluoride). An alternative procedure uses moderately expensive diethyl chlorophosphate but additionally requires the hazardous (pyrophoric) base sodium hydride to effect elimination.

Thus there is a need for an improved single step dehydration process which uses reagents which are readily available, inexpensive and non-hazardous. The present invention provides such a process.

Benefits:

Single step dehydration process that uses reagents which are readily available, inexpensive, and non-hazardous.

Applications:

- Pharmaceutical
- Flavors/Fragrances
- Agrichemical